

## WEST Search History

DATE: Sunday, December 23, 2007

Hide?	Set Name	Query	Hit Count
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L13	L12 and hematocrit	18
<input type="checkbox"/>	L12	L11 and @ay<2002	57
<input type="checkbox"/>	L11	L10 and neuron	161
<input type="checkbox"/>	L10	L9 and (protection or survival)	508
<input type="checkbox"/>	L9	(recombinant or mutein or mutant) near2 erythropoietin	1094
<input type="checkbox"/>	L8	erythropoietin and (protection or viability or survival)	11598
<i>DB=USPT,PGPB; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L7	CERAMI-CARLA!	14
<input type="checkbox"/>	L6	CERAMI-ANTHONY!	185
<input type="checkbox"/>	L5	BRINES-MICHAEL!	13
<input type="checkbox"/>	L4	CHRISTENSEN-SOREN!	11
<input type="checkbox"/>	L3	KALLUNKI-PEKKA!	9
<input type="checkbox"/>	L2	LEIST-MARCEL!	3
<input type="checkbox"/>	L1	NIELSEN-JACOB!	37

END OF SEARCH HISTORY

Can 10/612665  
WEST AD  
12/23/07

Case# 10/612665  
12/23/07 AD

FILE 'MEDLINE' ENTERED AT 13:27:00 ON 23 DEC 2007

FILE 'BIOSIS' ENTERED AT 13:27:00 ON 23 DEC 2007  
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=> s erythropoietin and (protection or viability or survival)  
L1 8227 ERYTHROPOIETIN AND (PROTECTION OR VIABILITY OR SURVIVAL)

=> s (recombinant or mutein or mutant) near2 erythropoietin  
MISSING OPERATOR MUTANT) NEAR2  
The search profile that was entered contains terms or  
nested terms that are not separated by a logical operator.

=> s (recombinant or mutein or mutant) (p) erythropoietins  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'MUTANT) (P) ERYTHROPO'  
L2 183 (RECOMBINANT OR MUTEIN OR MUTANT) (P) ERYTHROPOIETINS

=> s l2 (p) (protection or survival)  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L13 (P) '  
L3 9 L2 (P) (PROTECTION OR SURVIVAL)

=> dup rem l3  
PROCESSING COMPLETED FOR L3  
L4 4 DUP REM L3 (5 DUPLICATES REMOVED)

=> s l4 and neuron  
L5 0 L4 AND NEURON

=> disp l4 ibib abs 1-4

L4 ANSWER 1 OF 4 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights  
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ACCESSION NUMBER: 2007475423 EMBASE  
TITLE: Current approach in the use of erythropoietin.  
AUTHOR: Costa E.C.; Martin E.G.; Vilaplana P.G.  
CORPORATE SOURCE: P.G. Vilaplana, Servicio de Oncologia Medica, Institut  
Clinic de Malalties Hemato-Oncologiques (ICMHO), Hospital  
Clinic, Villarroel, 170, 08036 Barcelona, Spain.  
gascon@clinic.ub.es  
SOURCE: Cancer and Chemotherapy Reviews, (Apr 2007) Vol. 2, No. 2,  
pp. 121-132.  
Refs: 64  
ISSN: 1885-740X  
COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 016 Cancer  
025 Hematology  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index

## 038 Adverse Reactions Titles

LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20 Nov 2007  
Last Updated on STN: 20 Nov 2007

AB Anemia is a common side effect or treatment-related complication in cancer patients. It is associated with decreased quality of life, particularly as a result of fatigue, and a shorter survival time. In a pivotal study of the European Cancer Anemia Survey (ECAS), anemia occurred in 67% of the more than 15,000 patients analyzed. Management of cancer-related anemia has been redefined over the last decade to include administration of recombinant erythropoietins as a therapeutic modality. These agents are highly effective to increasing hemoglobin, decreasing transfusion utilization, and improving quality of life. Several studies have been published reporting the efficacy of these new agents in the oncology setting. This article provides an update on the current use of recombinant erythropoietins, including available treatment options (epoetin- $\alpha$ , epoetin- $\beta$ , and darbepoetin- $\alpha$ ), goals of treatment guidelines, safety, and future areas of investigation, with the aim of providing practical information to guide optimal anemia management in patients with cancer. Epoetin- $\alpha$  and epoetin- $\beta$  have identical amino acid sequence of isolated endogenous human erythropoietin. Epoetin- $\beta$  differs from epoetin- $\alpha$  in isoform composition and in the structure of its carbohydrate moieties. Darbepoetin- $\alpha$  was developed by mutating the erythropoietin gene to create two additional sites for glycosylation and increasing its proportion of sialic acid-containing carbohydrate, giving the molecule a longer half-life. The clinical significance of the pharmacologic differences between epoetin- $\alpha$ , epoetin- $\beta$ , and darbepoetin- $\alpha$  has yet to be determined. Evidence from clinical trials and experience in the general cancer population, as well as published guidelines, encourage treatment of patients who are symptomatic (including those displaying impaired quality of life) if their hemoglobin levels decline below 11 g/dl, with a goal of maintaining a level of about 12 g/dl. No predictive factors for hematopoietic response to erythropoietic agents have been validated in prospective trials. The greatest incremental improvement in quality of life occurs when hemoglobin levels increase from 11 to 12 g/dl (range: 11-13 g/dl). Recent studies have examined the clinical benefit of early interventions (mean baseline Hb > 10 g/dl) with epoetin- $\alpha$  and epoetin- $\beta$  to achieve rapid correction and/or maintenance of hemoglobin levels around 12 g/dl. The use of concomitant iron to compensate for the so-called functional iron deficiency is still controversial, although recent publications do suggest a clinical benefit if iron is given intravenously. Finally, several meta-analyses have been conducted to study the safety of erythropoietin use, in particular the issue of erythropoietin including tumor growth. Results from these meta-analyses failed to prove a negative impact on survival in patients receiving erythropoietin treatment. The consensus position on this concern is that erythropoietin administration is safe as long as it is given according to the registry specifications. Advances in the treatment of cancer have resulted not only in higher cure rates, but also in longer periods of survival for many patients with incurable disease. Under these circumstances, improving patient quality of life is often considered as important as improving the overall quantity of life.

L4 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2006181221 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16520805  
TITLE: Cancer-related anemia and recombinant human erythropoietin--an updated overview.  
AUTHOR: Bohlius Julia; Weingart Olaf; Trelle Sven; Engert Andreas  
CORPORATE SOURCE: Cochrane Haematological Malignancies Group, University of Cologne, Cologne, Germany.

SOURCE: Nature clinical practice. Oncology, (2006 Mar) Vol. 3, No. 3, pp. 152-64. Ref: 92  
Journal code: 101226509. ISSN: 1743-4254.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200607  
ENTRY DATE: Entered STN: 4 Apr 2006  
Last Updated on STN: 28 Jul 2006  
Entered Medline: 27 Jul 2006

AB For cancer patients, anemia can be a debilitating problem that negatively influences their overall quality of life and worsens their prognosis. The condition is caused either by the cancer itself or by cytotoxic treatment. Anemia is the primary indication for transfusion of red blood cells, but the development of recombinant human erythropoietins (epoetins) provides an alternative to red blood cell transfusions. Treatment with epoetins has been shown to reduce transfusion rates and increase hemoglobin response. There is some evidence that epoetins improve quality of life. It remains unclear, however, whether erythropoietin affects tumor growth and survival, and this area requires further investigation. Data from clinical trials suggest that erythropoietin increases the risk of thromboembolic complications. In the management of anemic patients, physicians should follow closely the dosing recommendations in products' package inserts or the ASCO/American Society of Hematology guidelines. Treatment of patients beyond the correction of anemia, however, has to be regarded as experimental and is potentially harmful, so should only be conducted in clinical trials.

L4 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2006167467 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16556069  
TITLE: Epoetin beta in oncology: examining the current evidence.  
AUTHOR: Ludwig Heinz  
CORPORATE SOURCE: Department of Medicine, Center for Oncology and Hematology, Wilhelminenspital, Montleartstr. 37, A-1171 Vienna, Austria.. heinz.ludwig@wienkav.at  
SOURCE: Future oncology (London, England), (2006 Feb) Vol. 2, No. 1, pp. 21-38. Ref: 108  
Journal code: 101256629. ISSN: 1479-6694.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200609  
ENTRY DATE: Entered STN: 25 Mar 2006  
Last Updated on STN: 23 Sep 2006  
Entered Medline: 22 Sep 2006

AB Anemia is highly prevalent in patients with cancer and its impact on quality of life and long-term outcome in these patients is well documented. Recombinant human erythropoietins, or epoetins, have been used to treat cancer-related or antitumor therapy-induced anemia for many years. Through a combination of clinical studies and extensive experience in the real-life clinical setting, epoetin beta has been shown to be efficacious and well tolerated, increasing hemoglobin levels, reducing the need for transfusion and improving quality of life. This favorable efficacy and safety profile has been demonstrated across a broad range of malignancy types, irrespective of the treatment used (platinum or non-platinum based). The effect of treatment with epoetin beta is rapid, with mean hemoglobin increases of 1 g/dl seen as early as 4 weeks following the start of therapy.

Furthermore, there is no evidence that epoetin beta negatively affects overall survival or tumor progression in anemic patients with cancer. The approved 30,000 IU once-weekly dosing regimen (as opposed to the 10,000 IU three-times weekly regimen) provides greater convenience and may result in improved treatment compliance.

L4 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2005499599 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15958437  
TITLE: Recombinant human erythropoietin in oncology: current status and further developments.  
AUTHOR: Engert A  
CORPORATE SOURCE: Klinik I fur Innere Medizin, Universitätsklinikum Koln, Koln, Germany.. a.engert@uni-koeln.de  
SOURCE: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, (2005 Oct) Vol. 16, No. 10, pp. 1584-95. Electronic Publication: 2005-06-15. Ref: 80  
Journal code: 9007735. ISSN: 0923-7534.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200601  
ENTRY DATE: Entered STN: 21 Sep 2005  
Last Updated on STN: 27 Jan 2006  
Entered Medline: 26 Jan 2006  
AB Anaemia effects up to 90% of cancer patients, with more than 60% requiring blood transfusion during or after treatment. With the advent of recombinant human erythropoietins (rHuEPO), an alternative to red blood cell transfusion has become available. So far, three drugs have been approved for the treatment of anaemia in patients with malignancies (epoetin alfa, epoetin beta and darbepoetin alfa). New concepts for the use of erythropoietin in cancer patients include 3- and 4-weekly dosing, as well as loading-dose concepts. Important factors helping to judge the impact of erythropoietin in cancer treatment include pharmacoeconomics and better predictive factors. Lately, the influence of erythropoietin therapy on survival in cancer patients has been discussed very intensively, because conflicting data have emerged. Studies aimed at correcting anaemia in cancer patients had indicated a possible survival advantage of those patients receiving erythropoietin. In contrast, two recent trials aimed at correction of haemoglobin levels beyond anaemia reported a poorer survival of patients receiving erythropoietin. This might grossly be attributed to a higher risk of thrombosis in these patients. The largest systematic review on the use of erythropoietin in cancer patients undergoing treatment indicates a suggestive but not significant survival advantage of erythropoietin-treated patients. In addition, very recent results of a Food and Drug Administration meeting on safety and survival of patients treated with erythropoietin are presented.

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